We Claim

~~CLAIMS~~

1. A PLB deactivating compound comprising any three of the following:

(a) a first electronegative moiety being capable of associating with the S1 binding site of the PLB cytosolic domain when the deactivator is bound thereto said binding site comprising Tyr-6, Arg-9 and/or Arg-13,
(b) a second electronegative moiety being capable of associating with the S2 binding site of the PLB cytosolic domain when the deactivator is bound thereto said binding site comprising Arg-14,
(c) a first hydrophobic moiety being capable of associating with the S3 binding site of the PLB cytosolic domain when the deactivator is bound thereto said binding site comprising Met-20, Lys-27 and/or Leu-28, and
(d) a second hydrophobic moiety being capable of associating with the S4 binding site of the PLB cytosolic domain when the deactivator is bound thereto said binding site comprising Phe-32 and/or Phe-35;
provided that the compound is not 3-benzyl-5,7-bis((1H-tetrazol-5-yl)-methyloxy)-4-methyl-2H-1-benzopyran-2-one.

2. A compound of claim 1 comprising any three of the following:

(a) a first electronegative moiety being capable of forming a hydrogen bond with the -OH group of Tyr-6, a salt bridge with the guanidinium group of Arg-9 and/or a salt bridge with the guanidinium group of Arg-13, of the PLB cytosolic domain when the deactivator is bound thereto,
(b) a second electronegative moiety being capable of forming a salt bridge with the guanidinium group of Arg-13, of the PLB cytosolic domain when the deactivator is bound thereto,
(c) a first hydrophobic moiety being capable of associating with a hydrophobic pocket created by Met-20, Lys-27 and/or Leu-28, of the PLB cytosolic domain when the deactivator is bound thereto, and
(d) a second hydrophobic moiety being capable of associating with a hydrophobic pocket created by Phe-32 and/or Phe-35, of the PLB cytosolic domain when the deactivator is bound thereto.

3. A compound of ~~claim 1~~ comprising
(a) a first electronegative moiety being capable of forming a hydrogen bond with the -OH group of Tyr-6, a salt bridge with the guanidinium group of Arg-9 and/or a salt bridge with the guanidinium group of Arg-13, of the PLB cytosolic domain when the deactivator is bound thereto,

(b) a second electronegative moiety being capable of forming a salt bridge with the guanidinium group of Arg-13, of the PLB cytosolic domain when the deactivator is bound thereto and
(c) a first hydrophobic moiety being capable of associating with a hydrophobic pocket created by Met-20, Lys-27 and/or Leu-28, of the PLB cytosolic domain when the deactivator is bound thereto.

4. A method of deactivating PLB which comprises administering to a mammal in need thereof a compound of Claim 1.

5. A pharmaceutical composition comprising a compound of Claim 1 as the active ingredient in admixture with a pharmaceutically acceptable carrier.

6. A method for identifying a PLB deactivator comprising the steps of:
i) providing atom coordinates of the structure of PLB cytosolic domain or portion thereof in a computerized modeling system, ii) identifying compounds which are capable of interacting with said structure, and iii) testing the compounds identified or analogs derived therefrom for the activation of CaATPase in the presence of phospholamban.

7. A method for identifying a PLB deactivator comprising the steps of:
i) providing atom coordinates of the structure of PLB cytosolic domain or portion thereof in a conformation which allows binding of a PLB deactivator to PLB cytosolic domain, in a computerized modeling system, ii) identifying compounds which are capable of said interaction iii) testing the compounds identified or analogs derived therefrom for the activation of CaATPase in the presence of phospholamban.

8. A computer readable medium having stored therein atom coordinates of the structure of the PLB cytosolic domain or portion thereof in a conformation which allows binding of a PLB deactivator to the PLB cytosolic domain.

9. A cyclic peptide having the structure:

Cys-X-Trp-Glu-Leu-Glu-Trp-Leu-Pro-Cys-Ala (pI)

10. A peptide of claim 7 wherein X is Tyr or Ala.